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EXAMINER	
HOWARD, ZACHARY C	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,692	JACOBSON ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-10,19,21,23-29 and 31-38* is/are pending in the application.

4a) Of the above claim(s) *1-5,7-10,19,21,24-29 and 31-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-5,7-10,19,21,23-29 and 31-38* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/8/07;8/10/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

Claims 1-5, 7-10, 19, 21, 23-29 and 31-38 are pending in the instant application.

Election/Restrictions

Claim 34 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 4, 5, 8-10, 19, 21, 24-27, 29 and 34 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

In the Office Action mailed 6/11/08, three additional elections of species were required. The following elections in the reply filed on 7/14/08 are acknowledged.

(1) Applicants' election of (b) methods wherein the test cell population is contacted with the test compound independently from the control cell population being contacted with the test compound as the species of method. Applicants state that claims 23, 28, 31-33 and 35-38 read upon this elected species. The Examiner agrees. Claims 1-3 and 7 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

(2) Applicants' election of (a) methods to identify an agonist of a metabotropic glutamate receptor as the species of method. Applicants state that claims 1-3, 7, 23, 28, 33, 37 and 38 read upon this elected species. The Examiner agrees. Claims 31, 32, 35 and 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

(3) Applicants' election of (a) measuring fluorescence of a calcium sensitive dye as the species of means for detecting a change in the elected measurable cellular response (intracellular calcium concentration). Applicants state that claims 1-3, 7, 23 and 35-38 read upon this elected species. The Examiner agrees. Claims 28 and 31-33

are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

On further consideration by the Examiner of the teachings of the relevant art, the species election with respect to the metabotropic glutamate receptor (mGluR) is withdrawn (Election of Species #1 at page 4 of the 1/23/08 Office Action). The claims directed to particular mGluR species (claims 25 and 26) remain withdrawn because they are directed to a non-elected species of method (i.e., they are limited to identification of negative modulators (antagonists), which is a non-elected species of method).

Claims 23, 37 and 38 are under consideration, as they are directed to the elected species of (1) change in intracellular calcium concentration; (2) methods wherein the test cell population is contacted with the test compound independently from the control cell population being contacted; (3) methods to identify an agonist of a metabotropic glutamate receptor; and (4) measuring fluorescence of a calcium sensitive dye as the means for detecting a change in intracellular calcium concentration.

Specification

The disclosure is objected to because of the following informalities:

(1) The title of the invention is not descriptive because it is broadly directed to any "cell surface receptor", whereas the claims are directed to metabotropic glutamate receptors. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: “METHODS FOR IDENTIFYING METABOTROPIC GLUTAMATE RECEPTOR MODULATORS”.

(2) The Brief Description of Figures 3 and 4 on page 14 are objected to because they appear to be reversed with respect to Figures 3 and 4. Specifically, Figure 3 is titled "Beta lactamase gene reporter assay with mGluR5 antagonist" and shows the cellular responses in the presence of the compounds quisqualate and MPEP. Figure 4 is titled "Beta-lactamase gene reporter assay with mGluR5 agonist and positive potentiator". However, in the specification the description of Figure 3 (pg 14) states "Dose response of the mGLUR5 agonist quisqualate in the absence ... and presence ... of … positive allosteric modulator", which appears to describe Figure 4 (i.e., Figure 4

but not Figure 3 includes a "positive potentiator"). The description of Figure 4 (pg 14) states "Assay of mGluR5 antagonist, MPEP, in the β-lactamase reporter gene assay ..." which appears to describe Figure 3 (i.e., Figure 3 but not Figure 4 includes MPEP).

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23, 37 and 38 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for:

a method of claim 23 wherein step (a) is (a) providing a cell population comprising a plurality of recombinant test cells modified to contain the DNA of (i) at least one naturally-occurring mammalian glutamate receptor subtype and (ii) a functional naturally-occurring non-human glutamate transporter protein; or

a method of claim 37 wherein the test cell population comprises a plurality of cells co-transfected with a nucleic acid encoding a naturally-occurring metabotropic glutamate receptor and a functional naturally-occurring glutamate transporter protein; or

a method of claim 38 wherein the cells co-express on their cell surface at least one naturally-occurring metabotropic glutamate receptor subtype and a naturally-occurring glutamate transporter protein specific for a ligand bound by said receptor;

does not reasonably provide enablement for

a method of claim 23 wherein step (a) is (a) providing a cell population comprising a plurality of recombinant test cells modified to contain the DNA of (i) at least one mammalian glutamate receptor subtype, or a variant, fragment or functional equivalent thereof and (ii) a functional non-human neurotransmitter protein or a variant, fragment or functional equivalent thereof, specific for a ligand of said receptor;

a method of claim 37 wherein the test cell population comprises a plurality of cells co-transfected with a nucleic acid encoding a metabotropic glutamate receptor and a functional glutamate transporter protein; or

a method of claim 38 wherein the cells co-express on their cell surface at least one metabotropic glutamate receptor subtype and a glutamate transporter protein specific for a ligand bound by said receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is “undue” include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention (as drawn to the elected species) is a method of screening candidate compounds to identify an agonist of a metabotropic glutamate receptor (mGluR), using cells expressing said receptor and a glutamate transporter.

The specification provides the following working examples. As described on page 13-14 of the specification, Figure 1 shows that three compounds (quisqualate, glutamate and 3,5-DHreceptor subtype 5 (mGluR5) and a murine glutamate transporter (mGLAST), as compared to a control in the absence of a test compound (baseline activity). Figure 2 shows the "Effect of mGLAST expression in mGluR5CHONFAT cells on basal activity of βlactamase gene reporter" and further teaches that "The co-expression of mGLAST in the mGluR5CHONFAT cells decreased the background by eliminating endogenous glutamate and allows for the measurement of receptor activation by exogenously added agonists" (pg 14). Figures 3 and 4 show results from further assays using the β-lactamase gene reporter in the presence of an antagonist (MPEP) or a "positive potentiator" (name/structure not disclosed).

The specification teaches that "[t]he term "receptor", as used herein, encompasses both naturally occurring and mutant receptors" (¶ 140 of the published application). Claim 23 explicitly encompasses "a variant, fragment or functional equivalent" mGluR receptor. Claims 37 and 38 each recite a "metabotropic glutamate receptor subtype", which in view of the definition of receptor in the specification includes both naturally occurring and mutant receptors. Thus, each of claims 23, 37 and 38 encompasses both naturally occurring and mutant mGluR receptors. Furthermore, for the same reasons, each of claims encompasses both naturally occurring and mutant glutamate transporter protein. The description of the figures in the specification does not specifically indicate whether the receptor (mGluR5) and transporter (mGLAST) used in the assays are naturally occurring or mutant receptors. However, in the absence of other teachings directing use of a specific mutant, the skilled artisan would assume that each is a naturally occurring sequence.

While the specification and claims each envision use of mutant proteins in the claimed methods, no guidance as to provided as mutations in mGluR and/or glutamate transporter proteins that can be made without destroying the functionality. Claim 23 requires "functional equivalents" of glutamate receptors and claim 37 requires a "functional glutamate transporter protein". However, even in the absence of a specific recitation of a "functional" receptor in the claims, the method of each claim requires a functional receptor for success.

The claims place no limitation on the number of mutations that may be present in a mGluR and/or glutamate transporter. The specification does not disclose any actual or prophetic examples on expected performance parameters of any of the possible variants of a naturally occurring mGluR and/or glutamate transporter sequence. The specification has not provided a working example of the use of a variant of a naturally occurring mGluR and/or glutamate transporter sequence, nor sufficient guidance so as to enable one of skill in the art to make such a variant. The specification has failed to teach which amino acids could be modified so as to produce a polypeptide that is not identical and yet still retain a characteristic of the parent polypeptide. Applicants have not given any guidance as to which amino acid substitutions, deletions or insertions to

make to achieve any desired property, or defined a difference in structure, or difference in function, between the protein corresponding a naturally occurring mGluR and/or glutamate transporter sequence and variants of said protein. If a variant of the protein corresponding is to have a structure and function similar to a naturally occurring mGluR and/or glutamate transporter sequence then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Particular regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et al*. (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified

in the specification, it may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39; Doerks *et al*. (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics **15**(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in sequence databases but watch out for the traps." Trends in Genetics **12**(10): 425-427].

Due to the large quantity of experimentation necessary to generate the large number of variants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

In addition, claim 23 lacks enablement for the full scope of the recitation "a functional non-human neurotransmitter protein or a variant, fragment or functional equivalent thereof, specific for a ligand of said receptor" because the specification fails to teach any such neurotransmitter other than a glutamate transporter. Due to the large quantity of experimentation necessary to identify any such neurotransmitter other than glutamate receptor, the lack of direction/guidance presented in the specification regarding the identify of such neurotransmitters, the absence of working examples

directed to same, the complex nature of the invention, the state of the prior art which fails to teach any such neurotransmitters, and the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by Coleman et al, WO 01/56990, published 9 August 2001.

The recitation of “for determining whether a chemical compound specifically binds to and activates one or more metabotropic glutamate receptor subtypes” in the preamble of claim 38 is interpreted as an intended use and bears no accorded patentable weight to distinguish a claimed method over one from the prior art. Accordingly, claim 38 encompasses any method that comprises "contacting cells producing a second messenger response and co-expressing on their cell surface at least one metabotropic glutamate receptor subtype and a glutamate transporter protein specific for a ligand bound by said metabotropic glutamate receptor subtype, with the chemical compound under conditions suitable for activation of the human metabotropic glutamate receptor and measuring the second messenger response in the presence and absence of the chemical compound, wherein a change in the second messenger response in the presence of the chemical compound indicates that the compound activates the metabotropic glutamate receptor subtype".

Coleman et al teach "[c]ell lines expressing human $mGlu_2$ receptors" and "these cells are referred to as RGT cells for Rat Glutamate Transporter, and have been co-transfected with the glutamate/aspartate transporter GLAST" (pg 195). The $mGlu_2$ receptor is the metabotropic glutamate receptor subtype 2. GLAST is a "glutamate transporter protein specific for a ligand bound by said metabotropic glutamate receptor

subtype" because it is specific for glutamate (a ligand bound by the glutamate receptor subtype). Coleman et al teach that the "RGT cell line expressing the $mGlu_2$ receptors was stably transfected with the promiscuous G-protein, Galpha15 to change the signaling pathway to the $mGlu_2$ to one that could be easily measured through release of intracellular calcium. Thus, intracellular calcium levels were monitored before and after the addition of drugs on a Fluorometric Imaging Plate Reader (i.e., FLIPR, Molecular Devices)" (pg 195). Coleman et al teach that the cells were loaded with "a calcium sensitive dye" named Fluo-3 (pg 195). Coleman et al teach "the compounds of formula I potentiate the response of the $mGlu_2$ receptor to glutamate". Thus, Coleman teaches a method of contacting cells producing a second messenger response (intracellular calcium release) and co-expressing the $mGlu_2$ receptor and the GLAST glutamate transporter with a chemical compound (formula I) under conditions suitable for activation of the receptor and measuring said response in the presence and absence of said compound (i.e., "before and after the addition of drugs") and wherein the change in the response in the presence of the compound indicates that the compound activates said receptor (i.e., "the compounds of formula I potentiate the response"). Thus, the teachings of Coleman anticipate claim 38.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coleman et al (WO 01/56990, published 8/9/01) and further in view of Negulescu et al (US Patent No 6,004,808, published 12/21/99).

The recitation of “for identifying a modulator of one or more mammalian metabotropic glutamate receptor subtypes” in the preamble of claim 23 is interpreted as an intended use and bears no accorded patentable weight to distinguish a claimed

method over one from the prior art. Accordingly, claim 23 encompasses any method that comprises specific method steps (a)-(g) recited in the claim. The teachings of Coleman described above meet each of steps (a)-(d) of claim 23. Coleman et al teach that the RGT cells expressing $mGlu_2$ were produced according to Desai et al (1995; cited previously). Desai et al disclose use of a mammalian expression vector pGT-h for mGlu expression (pg 649). Therefore, Coleman et al teach cells that meet the limitations of part (a), because they contain the DNA of (i) at least one mammalian glutamate receptor subtype ($mGlu_2$) which is operably linked to control sequences for expression (vector pGT-h) and whose activation can be coupled to a Ca^{2+} signaling pathway (the promiscuous G protein couples $mGlu_2$ to a calcium signaling pathway), and (ii) a functional non-human neurotransmitter protein specific for a ligand of said receptor (rat GLAST, which is neurotransmitter protein specific for glutamate). Coleman et al further teach contacting said cells with a test compound (formula I) and a calcium sensitive-fluorescent dye (Fluo-3), which meets the limitations of steps (b) and (c). Coleman et al further teach measuring the response of the cells to the test compound using FLIPR, which meets the limitations of step (d). Coleman further teaches that "[c]ell lines expressing human $mGlu_2$ receptors were derived as previously described" in Desai et al, 1995 (cited previously). [Desai describes construction of the RGT cell line by transfection of AV12 cells with GLAST cDNA (pg 649) and that the RGT cells were subsequently transfected with a mGlu (pg 649). Thus, the RGT cells are control cells as recited in claim 37 because they express a functional glutamate transporter protein (GLAST) but do not express a metabotropic glutamate receptor protein (mGlu). Thus, Coleman describes a control cell population (the RGT cells that are used to produce RGT cells expressing the $mGlu_2$ receptor).]

Coleman does not teach steps (e)-(g) of claim 23, which include repetition of steps (a)-(e) with control cells lacking a functional metabotropic glutamate receptor protein and determination of the "positive modulator" (agonist) based on a greater response in the test cells (part (d)) as compared to the control cells (part (d) (rather than on comparison of the activity in the presence and absence of the compound, as in claim 38). Coleman et al describe RGT cells that lack functional metabotropic glutamate

receptor protein (and are thus transfected with mGlu2 for use in screening), but do not describe a screening method including contacting said cells with a candidate agent, or identification of a "positive modulator" (agonist) based on comparison to the response in said cells.

Negulescu et al teach methods that employ promiscuous G-proteins for use in identifying ligands of G-protein coupled receptors (see Abstract). Negelescu et al further teach assays for detecting agonist activity wherein the response of cells expressing a GPCR and the promiscuous G-protein are compared to control cells that express the promiscuous G-protein alone. See, for example, Figures 7A and 7B, which show the response in a "cell-based … calcium indicator assay (FURA-PE3)" (col 3, line 59-60). In Figure 7A, the agonist solution is added to "cells transfected by pCIS/Gα16 and Gs-receptor expression plasmids" (col 3, lines 63-64). In Figure 7B, the agonist solution was added to "cells transfected by both [sic] pCIS/Gα16 alone" (col 3, lines 66-67).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the assay of Coleman et al in view of the teachings of Negelescu et al by producing a RGT-control cell population that lacks the GPCR of interest ($mGlu_2$) but includes the promiscuous G-protein of interest (Gα15), and by determining that a test compound is an agonist by comparing the activity of the cells expressing $mGlu_2$ to the control cells lacking $mGlu_2$. The person of ordinary skill in the art would be motivated to do so to provide a control for the screening assay that confirms that the candidate compound is an agonist of $mGlu_2$ by confirming that the activity does not occur in the absence of $mGlu_2$. Further, a person of ordinary skill in the art would have a reasonable expectation of success because the parent RGT cells used by Coleman et al could be used as control cells as taught by Negelescu et al simply by transfecting them only with the vector encoding the Gα15 G-protein (which is taught by Coleman et al)

The recitation of "for determining whether a candidate compound is a metabotropic glutamate receptor agonist" in the preamble of claim 37 is interpreted as an intended use and bears no accorded patentable weight to distinguish a claimed method over one from the prior art. Accordingly, claim 38 encompasses any method

that comprises "contacting a control cell population, comprising cells that do no express a functional metabotropic glutamate receptor protein, and a test cell population, comprising a plurality of cells co-transfected with a nucleic acid encoding a metabotropic glutamate receptor under conditions favoring expression of the metabotropic receptor on a surface of said transfected cells and a functional glutamate transporter protein, with the candidate agent under conditions favoring activation of the metabotropic glutamate receptor and detecting any increase in human metabotropic glutamate receptor activity relative to a control cell population, wherein such increase indicates that the candidate agent is a metabotropic glutamate receptor agonist". The method of claim 37 fully encompasses the method of claim 23 as practiced with the particular receptor ($mGlu_2$) and transporter (GLAST) taught by Coleman et al. As such, claim 37 is rejected for the same reasons as claim 23.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Z. C. H./
Examiner, Art Unit 1646

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646